


INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference JAB 1732-PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/50697		International filing date (day/month/year) 07.10.2003	Priority date (day/month/year) 08.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D211/58			
Applicant JANSSEN PHARMACEUTICA N.V.			

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>	
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>	

Date of submission of the demand 31.03.2004	Date of completion of this report 16.09.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Diederer, J Telephone No. +31 70 340-1097



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International application No. PCT/EP 03/50697

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-82 as originally filed

Claims, Numbers

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-13
	No: Claims	
Inventive step (IS)	Yes: Claims	1-13
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-13
	No: Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
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International application No. PCT/EP 03/50697

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: WO 97/16440 A (JANSSEN PHARMACEUTICA NV ; JANSSENS FRANS
EDUARD (BE); SOMMEN FRANCOIS) 9 May 1997 (1997-05-09)

The present application deals with 1,4-di-piperidin-4-yl-piperazine derivatives having neurokinin antagonistic activity, in particular NK₁ antagonistic activity.

The closest prior art is disclosed in document D1. Document D1 describes 1-piperidin-4-yl-piperazines having tachykinin antagonistic activity, in particular substance P antagonistic activity (a neurokinin) and are therefore useful for the treatment of the same kind of diseases as the compounds of the present application.

The difference of the compounds of D1 with the compounds of the present application is that the compounds of the present application bear a piperidin-1-ALK-Y-ALK-L-4-yl group on the piperazine whereas the compounds of D1 bear a L group. In the closest case L in D1 is a directly bonded benzimidazole or benzimidazolidone in which the benzimidazole is further substituted by an alkyl group (closest case of the present application is where Y=bond, ALK=alkyl and L=H). The difference is that in D1 the compounds have a benzimidazole group where the compounds of the present application have a piperidine group.

The problem underlying the present application was to provide alternative compounds with neurokinin activity. A skilled person would not, starting from the subject-matter of D1, replace the benzimidazole group for a piperidine group as he would not have an incentive to do so.

Therefore is the subject-matter of the present application considered to involve an inventive step with regard to Article 33(3) PCT.